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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: Review of Phosmet Incident Reports

DP Barcode D251427, Chemical #059201, Reregistration

Case #0242

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BACKGROUND

The following data bases have been consulted for the poisoning incident data on the active ingredient Phosmet (PC Code: 059201):

1) OPP Incident Data System (IDS) - reports of incidents from various sources, including registrants, other federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992. Reports submitted to the Incident Data System represent anecdotal reports or allegations only, unless otherwise stated. Typically no conclusions can be drawn implicating the pesticide as a cause of any of the reported health effects. Nevertheless, sometimes with enough cases and/or enough documentation, risk mitigation measures may be suggested.

- 2) Poison Control Centers as the result of Data-Call-Ins issued in 1993, OPP received Poison Control Center data covering the years 1985 through 1992 for 28 organophosphate and carbamate chemicals. Most of the national Poison Control Centers (PCCs) participate in a national data collection system, the Toxic Exposure Surveillance System which obtains data from about 70 centers at hospitals and universities. PCCs provide telephone consultation for individuals and health care providers on suspected poisonings, involving drugs, household products, pesticides, etc. Subsequently, PCC data for all pesticides was purchased for the years 1993 through 1996. Residential cases (about 90% of the total) have been analyzed and presented in this review.
- 3) California Department of Food and Agriculture (replaced by the Department of Pesticide Regulation in 1991) California has collected uniform data on suspected pesticide poisonings since 1982. Physicians are required, by statute, to report to their local health officer all occurrences of illness suspected of being related to exposure to pesticides. The majority of the incidents involve workers, partly due to the tie in between physician payment under workers compensation and reporting. Information on exposure (worker activity), type of illness (systemic, eye, skin, eye/skin and respiratory), likelihood of a causal relationship, and number of days off work and in the hospital are provided.
- 4) National Pesticide Telecommunications Network (NPTN) NPTN is a toll-free information service supported by OPP. A ranking of the top 200 active ingredients for which telephone calls were received during calendar years 1984-1991, inclusive has been prepared. The total number of calls was tabulated for the categories human incidents, animal incidents, calls for information, and others.

PHOSMET REVIEW

I. <u>Incident Data System</u>

Please note that the following cases from the IDS do not have documentation confirming exposure or health effects unless otherwise noted.

Incident#706-1

A pesticide incident occurred in 1986, when a man was driving his car with the windows open and was exposed to phosmet, benomyl, and metiram that was applied by a plane to a nearby apple orchard. He experienced headaches, stiff and sore joints, dizziness, and eye problems about eight hours later and went to an emergency room where he and his clothes were washed. He is still experiencing multiple chemical sensitivity and is under a doctor's care. No further information on the disposition of the case was reported.

Incident#2496-1

A pesticide incident occurred in 1995, when groomers experienced headaches and blurred vision. No further information on the disposition of the case was reported.

Incident#4538-1

A series of pesticide incidents occurred in 1994 and 1995, when 155 pet owners and 12 veterinarian groomers were exposed to phosmet. The primary symptoms experienced included headaches, ocular irritation, flu-like symptoms, respiratory symptoms, disorientation, dermal irritation and rash, nausea, vomiting, and diarrhea. Most of the incidents (65%) involved accidental exposure and product misuse. Types of misuse reported included applying without gloves, use without proper dilution, use in poorly ventilated areas, accidental ingestion, spills, and direct contact with the dog before the product dried. No further information on the disposition of these cases was reported.

Incident#5225-1

A pesticide incident occurred in 1997, when a girl got phosmet dip over her entire body area and experienced headaches, weakness, lethargy, and muscle aches in the arms and neck. No further information on the disposition of the case was reported.

Incident#6661-1

A pesticide incident occurred in 1996, when a female was exposed to phosmet at a veterinary clinic without wearing gloves. Two years later she reported headaches, heart problems, nausea, vomiting, dizziness, and several other symptoms which she suspects are related to her earlier exposure. She has an unspecified preexisting immunosuppressant disease. No further information on the disposition of the case was reported.

II. Poison Control Center Data

Phosmet was one of 28 chemicals for which Poison Control Center (PCC) data were requested. The following text and statistics are taken from an analysis of these data; see December 5, 1994 memo from Jerome Blondell to Joshua First.

The 28 chemicals were ranked using two types of measures: (A) number and percent occupational and non-occupational adult exposures reported to PCCs requiring treatment, hospitalization, displaying symptoms or serious life-threatening effects; (B) the same measures for children under age.

A. Occupational and Non-occupational Exposure

There were a total of 2,548 phosmet cases in the PCC data base. Of these, 136 cases were occupational exposure; 101 (74.3%) involved exposure to phosmet alone and 35 (25.7%) involved exposure to multiple chemicals, including phosmet. There were a total of 1432 adult non-occupational exposures; 1350(94.3%) involved this chemical alone and 82 (5.7%) were attributed to multiple chemicals.¹

In this analysis, four measures of hazard were developed based on the Poison Control Center data, as listed below.

- 1. Percent of all accidental cases that were seen in or referred to a health care facility (HCF).
- 2. Percent of these cases (seen in or referred to HCF) that were admitted for medical care.
- 3. Percent of cases reporting symptoms based on just those cases where the medical outcome could be determined.
- 4. Percent of those cases that had a major medical outcome which could be defined as life-threatening or resulting in permanent disability.

Exposure to phosmet alone or in combination with other chemicals was evaluated for each of these categories, giving a total of 8 measures. A ranking of the 28 chemicals was done based on these measures with the lowest number being the most frequently implicated in adverse effects. Table 1 presents the analyses for occupational and non-occupational exposures.

¹ Workers who were indirectly exposed (not handlers) were classified as non-occupational cases.

Table 1. Measures of Risk From Occupational and Non-occupational Exposure to Phosmet Using Poison Control Center Data from 1985-1992^a

	Occupational Exposure	Non-occupational Exposure
Percent Seen in HCF		
Single chemical exposure	58.4 (68.2)	29.3 (44.0)
Multiple chemical exposure	62.5 (69.8)	30.2 (46.1)
Percent Hospitalized		
Single chemical exposure	10.2 (12.2)	8.1 (9.9)
Multiple chemical exposure	11.8 (14.3)	9.0 (12.6)
Percent with Symptoms		
Single chemical exposure	85.0 (85.8)	64.6 (74.0)
Multiple chemical exposure	84.4 (85.8)	66.2(75.2)
Percent with Life-threatening S	ymptoms	
Single chemical exposure	1.7 ^b (0.0)*6	0.1° (0.0)
Multiple chemical exposure	1.3 ^b (0.5)*7	0.2° (0.05)

a Extracted from Tables 2, 3, 5 and 6 in December 5, 1994 memo from Jerome Blondell to Joshua First; number in parentheses is median score for that category.

Compared to other organophosphate and carbamate insecticides, phosmet had similar or somewhat below median levels (Table 1). A higher percent of life-threatening symptoms was observed, but based on only one or two cases. For non-occupational exposure, one life-threatening case was reported for exposure to phosmet alone and two life-threatening cases were reported which involved exposure to phosmet and other products. Phosmet cases were less likely to be seen in a health care facility and slightly less likely to be hospitalized than the other insecticides. Among the non-occupational cases, phosmet was less likely to result in symptoms.

B. Exposure in Children

A separate analysis of the number of exposures in children five years of age and under from 1985-1992 was conducted. For phosmet, there were 980 incidents; 960 involved exposure to phosmet alone and 20 involved other pesticides as well. Compared to 14 other organophosphates and carbamates that 25 or more children were exposed to, phosmet cases were one and a half more times as likely to be seen in a health care facility and nearly twice as likely to be hospitalized. Symptoms occurred just as often for phosmet and there was one life-threatening case reported in children under age six.

Poison Control Center data 1993-1996

b The percents calculated here are based on a single case.

^c The percents calculated here are based on a two cases.

^{*} Top 25% of chemicals are ranked with a superscript of 1 to 7

More recent data from the the nation's Poison Control Centers (PCCs) has been analyzed to determine the risks associated with residential use of 13 organophosphate insecticides including phosmet. Some 64-67 Centers at hospitals or universities participated in the Toxic Exposure Surveillance System from 1993 through 1996 (Litovitz et al. 1994-1997).

The current review is based on 424,469 records of pesticide-related exposures (excluding cases exposed to multiple products, attempted suicides, malicious intent, and confirmed non-exposures) reported to Poison Control Centers participating in TESS from 1993 through 1996. Of the 424,469 exposures, 392,188 occurred in a residential setting and 62,915 of these (16%) were due to organophosphate pesticides and 1,242 (0.3%) were due to phosmet.

Most of the 13 organophosphates analyzed showed an increase in reporting from 1993 to 1996 which is principally or perhaps wholly related to increased participation by Poison Control Centers and greater coverage of the U.S. population. Phosmet, on the other hand, showed a 23% drop from 1993 to 1996. This drop may be due to declining sales, particularly to consumers.

Like other organophosphates, 38% of the exposures reported to Poison Control Centers involve children under six years of age. As in the analysis for 1985-92, residential exposures were examined proportionately to determine the likelihood of being seen in a health care facility, hospitalized, treated in an intensive care unit, developing symptoms, and developing life-threatening or fatal symptoms. Table 2 presents the results of these comparisons. Children exposed to phosmet were 2.4 times more likely to be seen in a health care facility than children exposed to non-organophosphate pesticides. Once in a health care facility, children were 4.8 times more likely to be hospitalized and 8.8 times more likely to be seen in an intensive care unit if exposed to phosmet than if exposed to a non-organophosphate. Ninety percent of exposures were due to flea-control products used on dogs (dog dips).

Table 2. Percent residential cases seen in a health care facility (HCF), percent hospitalized (of those seen in a HCF), percent treated in an intensive care unit (ICU), percent with related symptoms (where outcome was known), and percent with major or fatal medical outcome for children under age six, PCCs 1993-1996.

PESTICIDE	% in a HCF	% Hospit- alized	% ICU	% with symptoms	% major or fatal
PHOSMET	43.41*	22.0^{3}	10.31	24.6 ²	0.0
MEAN ALL OPs	12.7	15.2	6.6	23.0	0.4
MEAN NON-OPs	17.8	4.6	1.17	22.0	Ò.1

^{*} A superscript of 1-3 was used for the top 3 out of a total of 13 organophosphate insecticides with widespread residential exposures.

Though not as dramatic, a similar increase in hazard was observed for adults and older children handling phosmet as shown in Table 3.

Table 3. Percent residential cases seen in a health care facility (HCF), percent hospitalized (of those seen in a HCF), precent treated in an intensive care unit, percent with related symptoms (where outcome was known), and percent with major or fatal medical outcome for adults and children 6-19 years old, PCCs 1993-1996.

PESTICIDE	% in a % Hospit- % HCF alized		% ICU	% with symptoms	% major or fatal	
PHOSMET	25.4 ¹	13.8 ²	6.6	65.0	0.0	
MEAN ALL OPs	17.9	9.9	4.7	69.5	0.3	
MEAN NON-OPs	17.6	6.6	2.72	70.7	0.3	

A superscript of 1 to 3 was used for the top 3 out of a total of 13 organophosphate insecticides with widespread residential exposures.

A primary measure of hazard is the incident rate defined as the number of individuals who become ill divided by the number at risk over some time period. Tables 2-3 look at proportionate hazard which is one way of ranking pesticides by their potential for causing problems. Another method is to develop a surrogate measure for the population at risk by estimating the extent of pesticide use in residential households. The EPA survey of home and garden pesticide use provides estimated number of containers and applications of pesticides for all households in the United States in 1990 (Whitmore et al. 1992). Table 4 takes all of the reported symptomatic cases in young children and adults/older children and estimates the rate of poisoning (cases defined as minor, moderate, major, or fatal outcome) per million containers and per million applications in U.S. homes. The purpose of this analysis is to determine whether widespread use rather than some other factor is responsible for a high hazard ranking.

Table 4 compares the number of symptomatic cases, those cases with a medical outcome of minor, moderate, major, or fatal, with the estimated use in households in 1990. Fenthion and propetamphos did not have any significant use reported in the 1990 survey of home and garden pesticide use. Both pesticides are applied mainly by professional applicators, especially fenthion which is used primarily for mosquito abatement. This table shows that the problems suggested in earlier tables for phosmet are not simply due to the widespread use. Phosmet ranked highest for three out of the four ratios in table 4.

Table 4. Ratio of residential symptomatic cases (outcome determined, average per year for 1993-1996) per million containers and per million applications in U.S. homes in 1990 for children five

years and under and adults and children older than five years.

	CHILD SYMP CASES PE		ADULT SYMPTOMATIC CASES PER USE					
PESTICIDE	MILLION MILLION APPLICA- CONTAINERS TIONS C		MILLION CONTAINERS	MILLION APPLICA- TIONS				
PHOSMET	60.01*	42.5¹	189.4¹	134.1 ²				
MEDIAN FOR 11 OPs	5.8	1.0	29.1	8.1				
MEAN ALL OPs	11.2	1.6	43.7	6.3				

^{*} A superscript of 1 to 3 was used for the top 3 out of a total of 11 organophosphate insecticides with widespread residential exposures.

In summary, phosmet ranked first for health care facility use, third for hospitalization, first for ICU use, and second for symptoms in children (Table 2). Phosmet ranked 1st for health care facility use and 2nd for hospitalization for adults (Table 3). Phosmet ranked 1st for ratio of poisoning per million containers and per million applications for children and per million containers for adults and it ranked 2nd per million applications for adults (Table 4).

Phosmet appears to pose a much greater risk to children than other organophosphate insecticides, primarily on account of the manner in which it is sold, a 12 percent concentrate that must be diluted 128-fold before being used as a pet dip for dogs. Based on estimated oral toxicity in animals, 1 swallow or 1 teaspoon of phosmet concentrate ingested by a 10 kg one-year old child could be a lethal dose. Adults are also at increased risk, probably because of failure to use protective clothing as required on the label.

III. California Data - 1982 through 1995

Detailed descriptions of 57 cases submitted to the California Pesticide Illness Surveillance Program (1982-1995) were reviewed. In 36 of these cases, phosmet alone was judged to be responsible for the health effects. Only cases with a definite, probable or possible relationship were reviewed. Phosmet ranked 46th as a cause of systemic poisoning in California. One individual was hospitalized between 1982 and 1995. Table 5 presents the types of illnesses reported by year. Table 6 gives the total number of workers that took time off work as a result of their illness and how many were hospitalized and for how long.

Table 5. Cases Due to Phosmet Exposure in California Reported by Type of Illness and Year, 1982-1995.

	Illness Type							
Year	Systemic ^a	Eye	Skin	Resp	Combination ^b	Total		
1982	1	1	-	-	-	2		
1983	2	-	-	-	-	2		
1984	4	-	***	<u>-</u>	-	4		
1985	1	_	· -	-	-	1		
1986	2	-	1	-	-	3		
1987	1	-	1	-	-	2		
1988	2	2	•	_	-	4		
1989	2	-	2	_	-	4		
1990	1	2	1	1	-	5		
1991	2	_	-	<u>-</u>	-	2		
1992	3	_	-	-	· -	3		
1993	3	_	-	-	-	3		
1994	_	-	-	-	-	-		
1995	1	-	_	•	_	1		
Total	25	5	5	1	-	36		

^a Category includes cases where skin, eye, or respiratory effects were also reported

A total of 25 persons had systemic illnesses or 69.4% of 36 persons. A variety of worker activities were associated with exposure to phosmet as illustrated in Table 7 below.

^b Category includes combined irritative effects to eye, skin, and respiratory system

Table 6. Number of Persons Disabled (taking time off work) or Hospitalized for Indicated

Number of Days After Phosmet Exposure in California, 1982-1995.

·	Number of Persons Disabled	Number of Persons Hospitalized					
One day	6	-					
Two days	3	-					
3-5 days	4	1					
6-10 days	-	<u>-</u>					
more than 10 days	-	-					
Unknown	2	-					

Table 7. Illnesses by Activity Categories for Phosmet Exposure in California, 1982-1995

	Illness Category						
Activity Category ^a	Systemic ^b	Eye	Skin	Resp.	Combination ^c	Total	
Applgrou	2	1	2	_	-	5	
Applother	10	1	2	-	_	13	
Driftexp	3	•		_	<u>.</u>	3	
Expotoco	2	-	-	1	-	3	
Mixload	1	2	-	-	-	3	
Nonocc	6	1	-	-	-	7	
Resifield	1	-	1	_	-	2	
Total	25	5	. 5	1	-	36	

^a Applgrou= ground applicator; Applother= applicator, other spray/dust application methods; Driftexp= exposure to pesticide that has drifted from intended targets; Expotoco= persons handling pesticide products between packaging and end-use; Mixload= mixer and/or loader of pesticide concentrates and dilute pesticides; Nonocc= other non-occupational exposure; Resifield= field worker exposed to residue in the field.

^b Category includes cases where skin, eye, or respiratory effects were also reported

^c Category includes combined irritative effects to eye, skin, and respiratory system

According to the above activity categories, applicators were associated with half of the exposures. A minimal number of cases involve spray drift or exposure to field residues. The illnesses included symptoms of lightheadedness, shortness of breath, difficulty breathing, slow heart beat, sweating, dizziness, rash on face and hands, numb hands, weight loss, and blurred vision.

Ratios of poisoning - California Data

The incidence of **systemic poisoning cases** in agricultural workers reported to the California was compared to the number of applications of phosmet. Those calculations, along with the median score for a total of 29 pesticides, are presented in the Table 8 below.

Table 8. Systemic Poisonings/1,000 Applications in Selected Agricultural Workers Exposed to Phosmet in California, 1982-1989^a

Pesticide	Number of Appl.		Poisonings/1,000 Appl. (N) Primary Pesticide Only			Poisonings/1,000 Appl.(N) Multiple Pesticide Exposure		
		Handlers	Field Workers	Total	Handlers	Field Workers	Total	
Phosmet	14,127	.07 (1)	.00 (0)	.07 (1)	.21 (3)	.07 (1)	.28 (4)	
Median		.21	.20	.41	.44	.50	1.02	

a Extracted from Table A5 in December 5, 1994 memo from Jerome Blondell to Joshua First; number in parentheses is the observed number of poisoned cases.

Phosmet had the ratios for handlers and field workers (poisonings per 1,000 applications) that were much lower than the median for 29 insecticides used widely in California when exposures to mixtures were included and excluded (See Table A5 in the December 5, 1994 memo.) The ratio for handlers, for example, was only one-third the median for all insecticides. These results should be interpreted with caution because they are based on a relatively small number of cases and applications.

IV. National Pesticide Telecommunications Network

On the list of the top 200 chemicals for which NPTN received calls from 1984-1991 inclusively, phosmet ranked 39th with 93 incidents in humans reported and 19 incidents in animals (mostly pets). From April 1995 through March 1998, the NPTN received approximately 13 calls concerning human health effects possibly related to phosmet. Only calls where phosmet was the only source of exposure or where it was the only cholinesterase inhibitor and the symptoms were consistent with cholinesterase inhibition were included. Half of the 14 calls involved groomers or persons using phosmet as a flea dip for dogs and experienced difficulty breathing, chest pain, nausea, headaches, dizziness, headaches, and respiratory problems. One

woman, who was a dog groomer for eighteen years, reported three miscarriages during that time which she thought might be related to her use of phosmet or pyrethrins. Two persons in separate incidents, were hospitalized for five days after dipping dogs and experienced weakness, nausea, dizziness, chest pain, and difficulty breathing. One of these two people reported difficulty walking for two weeks after her exposure.

The other half of the calls involved phosmet that was applied to a field or area and persons were exposed to the chemical. Three persons reported chronic symptoms such as persistent headaches, partial paralyzation, memory loss, difficulty concentrating, and neuropathy.

V. Literature Review

Ames et al. (1989) reported on a telephone survey conducted in California, March through August 1987, to determine whether health symptoms were associated with occupational exposure to flea control products among pet care facility workers. The survey was conducted of workers from veterinary clinics, pet stores, pet boarding kennels, pet grooming shops, and animal control facilities. Information was gathered on exposure to flea control products, industrial hygiene practices, protective clothing use, and symptoms that occurred three months prior to being interviewed. Six hundred and ninety-six employees (496 exposed and 200 unexposed) were interviewed and asked to report symptoms experienced, from a list of 45 symptoms, within the past three months. Among exposed employees, only 295 reported wearing rubber gloves and only 21% wore a protective apron. After applying flea control products, the following symptoms experienced were found to be statistically significant when comparing applicators to nonapplicators: skin rash, increased tearing, unusual tiredness, burning eyes, and flushing of skin after controlling for gender, current smoking status, and years of school completed. However, phosmet alone did not exhibit any statistically significant increase in symptoms frequency when compared to nonexposed workers at the same facility. It should be noted that 23% of the employers contacted for this study refused to cooperate which may have biased the results.

Good et al. (1993) reported on a fifty-one year old man who got phosmet on his face and hands and experienced diplopia, lightheadedness, a progressive staggering gait, dysphagia, change in voice tone, excessive diaphoresis, facial, jaw, and neck weakness, mild distal and proximal muscle weakness, and droopy eyelids. He experienced these symptoms after he was exposed to phosmet for the past five weeks and was admitted to the hospital five days later. On the ninth day of hospitalization, he experienced paralysis around the neck and shoulders, visual hallucinations, disorientation, and myoclonic jerks in his extremities which persisted for 10 days. The paralysis continued for 30 days, with some weakness persisting for about four months. His red blood cell cholinesterase level was normal upon admission and two and three weeks later. He was administered a nerve conduction and repetitive stimulation neuromuscular study while in the hospital. His motor responses were somewhat reduced in amplitude and prolonged in latency for the median, ulnar, and peroneal nerves. His neuromuscular exam was normal about five months later. The authors concluded that subacute neuromuscular syndrome can be experienced without marked symptoms of acute toxicity.

Rosenberg and Quenon (1988) reported two incidents on exposure to flea-dip products in September 1986. In one incident, a thirty-three year old woman, who is a pet groomer, experienced periodic headaches, nausea, dizziness, tiredness, blurred vision, sweating, confusion, and feeling spaced out. The woman treated dogs for 18 months (about 10 dogs a day in the summer) with products containing 11.6% phosmet and frequently spilled the concentrated chemical on her skin while diluting the product. Her red blood cell cholinesterase level was normal, however, symptoms diminished after atropine treatment. A telephone survey was conducted in September 1986 of twenty-four pet groomers by the California Health Department. The groomers were randomly selected from telephone directory lists in the San Francisco Bay and Los Angeles area. Twelve groomers reported symptoms, most commonly headache, dizziness, nausea, fatigue, and dermatitis. Flea-control products containing phosmet were most often reported as being related to the symptoms. Most groomers reported they did not wear aprons or gloves and often worked with undiluted concentrate with bare hands.

V. Conclusions

The majority of the more serious cases involved systemic illnesses to pet owners, groomers and veterinary assistants who were not properly protected and experienced illnesses while treating dogs for fleas, which is a misuse of the product. More importantly, a majority of groomers surveyed reported handling concentrate with bare hands, a clear pattern of widespread misuse. It appears unlikely that label warning requiring protective equipment will be followed by consumers using flea-control products on pets. Several poisoned cases report persistant symptoms that may last for months or years. This is consistent with cross-sectional studies which support the conclusion that organophosphates can lead to chronic neuro-behavioral effects in a subset of those poisoned (see Review of Diazinon Incident Reports, July 2, 1998, DP Barcode D245285, from Jerome Blondell and Monica Spann to Tim Leighton). Pet groomers and persons with several animals who may repeatedly dip their animals may be at greater risk for illness due to repeated exposure to the product. Two reports (Good et al. 1993 and Rosenberg and Quenon (1988) present patients with classic and relatively specific organophosphate symptoms but with normal red blood cell cholinesterase. These two studies suggest that red blood cell cholinesterase may not be a good indicator of phosmet poisoning. Agricultural use of phosmet is not associated with increased risk when compared to other organophosphate and carbamate insecticides.

VI. Recommendations

Data support the need for appropriate personal protective equipment such as gloves, a protective apron, and eye protection which should be mandatory. Surveys and incidents show a widespread pattern of misuse, therefore all flea-control products sold as liquid concentrates

should be restricted to use by a certifed applicator or someone under their supervision. Labels for products should advise that the area be well-ventilated while using the product. No specific recommendations are made for agricultural use of phosmet. Measures to reduce risk to applicators and handlers of phosmet should be consistent with other organophosphate and carbamates.

VII. References

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